



RECEIVED
JUL 31 2002
TECH CENTER 1600/2900

<110> CIEPLAK, WITOLD

<120> PERTUSSIN TOXIN GENE: CLONING AND EXPRESSION
PROTECTIVE ANTIGEN

<130> 2026-4253US7

<140> 09/770,875

<141> 2001-01-26

<150> 07/311,612

<151> 1989-02-15

<150> 07/542,149

<151> 1990-06-22

<150> 08/483,326

<151> 1995-06-07

<150> 09/128,911

<151> 1998-08-04

<160> 28

<170> PatentIn Ver. 2.1

<210> 1

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<212> DNA

<213> Bordetella pertussis

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cggcgcgatg acgcatttt ccccgccct ggcgcgacgtt ccttatgtgc tgggaagac 120
caatatggtg gtcaccagcg tagccatgaa gccgtatgaa gtcaccccg cgcggatgct 180
ggtc 184

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<211> 61

<212> PRT

<213> Bordetella pertussis

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Pro Gly Gln Gly Gly Ala Arg Arg Ser Arg Val Arg Ala Leu Ala Trp

1

5

10

15

Leu Leu Ala Ser Gly Ala Met Thr His Leu Ser Pro Ala Leu Ala Asp
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 Val Pro Tyr Val Leu Val Lys Thr Asn Met Val Val Thr Ser Val Ala
 35 40 45
 Met Lys Pro Tyr Glu Val Thr Pro Thr Arg Met Leu Val
 50 55 60

<210> 3

<211> 17

<212> DNA

<213> Bordetella pertussis

<220>

<223> Purine (P) R=G or A; Y=T or C; N=A, C, G, or T

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<222> (6)

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<222> (15)

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atgaarcnt aygargt

17

<210> 4

<211> 30

<212> PRT

<213> Bordetella pertussis

<220>

<223> Xaa = Any amino acid; the 8th Val and 4th Pro are questionable.

<220>

<221> VARIANT

<222> (15)

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Ala Met Lys Pro Tyr Glu Val Val Pro Pro Arg Met Leu Val
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<212> DNA

<213> Bordetella pertussis

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atcgctcctgc tcaaccgcca catcaacgag gcgctgcagt ccaaggcggt cgtcgaggcc 120

tttgccgccc aaggcgccac gccggtcatc gccacgcggg atcagaccgg cggtttcatc 180

gcagacgaga tccagcgctg ggccggcgctc gtgcgcgaaa ccggcgccaa gctgaagtag 240

cagcgcagcc ctccaacgcg ccatccccgt ccggccggca ccatccggca tacgtgttg 300

155

160

165

att ccg ccc gaa aac atc cgc agg gta acg cgg gtc tat cac aac ggc 1061
 Ile Pro Pro Glu Asn Ile Arg Arg Val Thr Arg Val Tyr His Asn Gly
 170 175 180 185

atc acc ggc gag acc acg acc acg gag tat tcc aac gct cgc tac gtc 1109
 Ile Thr Gly Glu Thr Thr Thr Thr Glu Tyr Ser Asn Ala Arg Tyr Val
 190 195 200

agc cag cat act cgc gcc aat ccc aac ccc tac aca tcg cga agg tcc 1157
 Ser Gln His Thr Arg Ala Asn Pro Asn Pro Tyr Thr Ser Arg Arg Ser
 205 210 215

gta gcg tcg atc gtc ggc aca ttg gtg cgc atg gcg ccg gtg ata ggc 1205
 Val Ala Ser Ile Val Gly Thr Leu Val Arg Met Ala Pro Val Ile Gly
 220 225 230

gct tgc atg gcg cgg cag gcc gaa agc tcc gag gcc atg gca gcc tgg 1253
 Ala Cys Met Ala Arg Gln Ala Glu Ser Ser Glu Ala Met Ala Ala Trp
 235 240 245

tcc gaa cgc gcc ggc gag gcg atg gtt ctc gtg tac tac gaa agc atc 1301
 Ser Glu Arg Ala Gly Glu Ala Met Val Leu Val Tyr Tyr Glu Ser Ile
 250 255 260 265

gcg tat tcg ttc tagacctggc ccagccccgc ccaactccgg taattcaaca gc 1355
 Ala Tyr Ser Phe

atg ccg atc gac cgc aag acg ctc tgc cat ctc ctg tcc gtt ctg ccg 1403
 Met Pro Ile Asp Arg Lys Thr Leu Cys His Leu Leu Ser Val Leu Pro
 270 275 280 285

ttg gcc ctc ctc gga tct cac gtg gcg cgg gcc tcc acg cca ggc atc 1451
 Leu Ala Leu Leu Gly Ser His Val Ala Arg Ala Ser Thr Pro Gly Ile
 290 295 300

gtc att ccg ccg cag gaa cag att acc cag cat ggc agc ccc tat gga 1499
 Val Ile Pro Pro Gln Glu Gln Ile Thr Gln His Gly Ser Pro Tyr Gly
 305 310 315

cgc tgc gcg aac aag acc cgt gcc ctg acc gtg gcg gaa ttg cgc ggc 1547
 Arg Cys Ala Asn Lys Thr Arg Ala Leu Thr Val Ala Glu Leu Arg Gly
 320 325 330

agc ggc gat ctg cag gag tac ctg cgt cat gtg acg cgc ggc tgg tca 1595
 Ser Gly Asp Leu Gln Glu Tyr Leu Arg His Val Thr Arg Gly Trp Ser
 335 340 345

ata ttt gcg ctc tac gat ggc acc tat ctc ggc ggc gaa tat ggc gc 1643
 Ile Phe Ala Leu Tyr Asp Gly Thr Tyr Leu Gly Gly Glu Tyr Gly Gly
 350 355 360 365

gtg atc aag gac gga aca ccc ggc ggc gca ttc gac ctg aaa acg acg 1691
 Val Ile Lys Asp Gly Thr Pro Gly Gly Ala Phe Asp Leu Lys Thr Thr
 370 375 380

ttc tgc atc atg acc acg cgc aat acg ggt caa ccc gca acg gat cac 1739
 Phe Cys Ile Met Thr Thr Arg Asn Thr Gly Gln Pro Ala Thr Asp His
 385 390 395

tac tac agc aac gtc acc gcc act cgc ctg ctc tcc agc acc aac agc 1787
 Tyr Tyr Ser Asn Val Thr Ala Thr Arg Leu Leu Ser Ser Thr Asn Ser
 400 405 410

agg cta tgc gcg gtc ttc gtc aga agc ggc caa ccg gtc att ggc gcc 1835
 Arg Leu Cys Ala Val Phe Val Arg Ser Gly Gln Pro Val Ile Gly Ala
 415 420 425

tgc acc agc ccg tat gac ggc aag tac tgg agc atg tac agc cgg ctg 1883
 Cys Thr Ser Pro Tyr Asp Gly Lys Tyr Trp Ser Met Tyr Ser Arg Leu
 430 435 440 445

cgg aaa atg ctt tac ctg atc tac gtg gcc ggc atc tcc gta cgc gtc 1931
 Arg Lys Met Leu Tyr Leu Ile Tyr Val Ala Gly Ile Ser Val Arg Val
 450 455 460

cat gtc agc aag gaa gaa cag tat tac gac tat gag gac gca acg ttc 1979
 His Val Ser Lys Glu Glu Gln Tyr Tyr Asp Tyr Glu Asp Ala Thr Phe
 465 470 475

gag act tac gcc ctt acc ggc atc tcc atc tgc aat cct gga tca tcc 2027
 Glu Thr Tyr Ala Leu Thr Gly Ile Ser Ile Cys Asn Pro Gly Ser Ser
 480 485 490

tta tgc tgagacgctt cccactcga accaccgccc cgggacaggg cggcgcccg 2083
 Leu Cys
 495

cggtcgcgc atg cgc gcc ctg gcg tgg ttg ctg gca tcc ggc gcg atg acg 2134
 Met Arg Ala Leu Ala Trp Leu Leu Ala Ser Gly Ala Met Thr
 500 505

cat ctt tcc ccc gcc ctg gcc gac gtt cct tat gtg ctg gtg aag acc 2182
 His Leu Ser Pro Ala Leu Ala Asp Val Pro Tyr Val Leu Val Lys Thr
 510 515 520 525

aat atg gtg gtc acc agc gtc gcc atg aag ccg tat gaa gtc acc ctg	2230
Asn Met Val Val Thr Ser Val Ala Met Lys Pro Tyr Glu Val Thr Pro	
530 535 540	
acg cgc atg ctg gtc tgc ggc atc gcc gcc aaa ctg ggc gcc gcg gcc	2278
Thr Arg Met Leu Val Cys Gly Ile Ala Ala Lys Leu Gly Ala Ala Ala	
545 550 555	
agc agc ccg gac gcg cac gtg ccg ttc tgc ttc ggc aag gat ctc aag	2326
Ser Ser Pro Asp Ala His Val Pro Phe Cys Phe Gly Lys Asp Leu Lys	
560 565 570	
cgt ccc ggc agc agt ccc atg gaa gtc atg ttg cgc gcc gtc ttc atg	2374
Arg Pro Gly Ser Ser Pro Met Glu Val Met Leu Arg Ala Val Phe Met	
575 580 585	
caa caa cgg ccg ctg cgc atg ttt ctg ggt ccc aag caa ctc act ttc	2422
Gln Gln Arg Pro Leu Arg Met Phe Leu Gly Pro Lys Gln Leu Thr Phe	
590 595 600 605	
gaa ggc aag ccc gcg ctc gaa ctg atc ccg atg gtc gaa tgc agc ggc	2470
Glu Gly Lys Pro Ala Leu Glu Leu Ile Arg Met Val Glu Cys Ser Gly	
610 615 620	
aag cag gat tgc ccc tgaaggcgaa cccc atg cat acc atc gca tcc atc	2520
Lys Gln Asp Cys Pro Met His Thr Ile Ala Ser Ile	
625 630	
ctg ttg tcc gtg ctc ggc ata tac agc ccg gct gac gtc gcc ggc ttg	2568
Leu Leu Ser Val Leu Gly Ile Tyr Ser Pro Ala Asp Val Ala Gly Leu	
635 640 645	
ccg acc cat ctg tac aag aac ttc act gtc cag gag ctg gcc ttg aaa	2616
Pro Thr His Leu Tyr Lys Asn Phe Thr Val Gln Glu Leu Ala Leu Lys	
650 655 660 665	
ctg aag ggc aag aat cag gag ttc tgc ctg acc gcc ttc atg tcg ggc	2664
Leu Lys Gly Lys Asn Gln Glu Phe Cys Leu Thr Ala Phe Met Ser Gly	
670 675 680	
aga agc ctg gtc ccg gcg tgc ctg tcc gac gcg gga cac gag cac gac	2712
Arg Ser Leu Val Arg Ala Cys Leu Ser Asp Ala Gly His Glu His Asp	
685 690 695	
acg tgg ttc gac acc atg ctt ggc ttt gcc ata tcc gcg tat gcg ctc	2760
Thr Trp Phe Asp Thr Met Leu Gly Phe Ala Ile Ser Ala Tyr Ala Leu	
700 705 710	

aag agc cgg atc gcg ctg acg gtg gaa gac tcg ccg tat ccg ggc t 2808
 Lys Ser Arg Ile Ala Leu Thr Val Glu Asp Ser Pro Tyr Pro Gly Thr
 715 720 725

ccc ggc gat ctg ctc gaa ctg cag atc tgc ccg ctc aac gga tat tgc 2856
 Pro Gly Asp Leu Leu Glu Leu Gln Ile Cys Pro Leu Asn Gly Tyr Cys
 730 735 740 745

gaa tgaacccttc cggaggtttc gacgtttccg cgcaatccgc ttgagacgat 2909
 Glu

cttccgcctt ggttccattc cgggaacacc gcaac atg ctg atc aac aac aag 2962
 Met Leu Ile Asn Asn Lys
 750

aag ctg ctt cat cac att ctg ccc atc ctg gtg ctc gcc ctg ctg ggc 3010
 Lys Leu Leu His His Ile Leu Pro Ile Leu Val Leu Ala Leu Leu Gly
 755 760 765

atg cgc acg gcc cag gcc gtt gcg cca ggc atc gtc atc ccg ccg aag 3058
 Met Arg Thr Ala Gln Ala Val Ala Pro Gly Ile Val Ile Pro Pro Lys
 770 775 780

gca ctg ttc acc caa cag ggc ggc gcc tat gga cgc tgc ccg aac gga 3106
 Ala Leu Phe Thr Gln Gln Gly Gly Ala Tyr Gly Arg Cys Pro Asn Gly
 785 790 795 800

acc cgc gcc ttg acc gtg gcc gaa ctg cgc ggc aac gcc gaa ttg cag 3154
 Thr Arg Ala Leu Thr Val Ala Glu Leu Arg Gly Asn Ala Glu Leu Gln
 805 810 815

acg tat ttg cgc cag ata acg ccc ggc tgg tcc ata tac ggt ctc tat 3202
 Thr Tyr Leu Arg Gln Ile Thr Pro Gly Trp Ser Ile Tyr Gly Leu Tyr
 820 825 830

gac ggt acg tac ctg ggc cag gcg tac ggc ggc atc atc aag gac gcg 3250
 Asp Gly Thr Tyr Leu Gly Gln Ala Tyr Gly Gly Ile Ile Lys Asp Ala
 835 840 845

ccg cca ggc gcg ggg ttc att tat cgc gaa act ttc tgc atc acg acc 3298
 Pro Pro Gly Ala Gly Phe Ile Tyr Arg Glu Thr Phe Cys Ile Thr Thr
 850 855 860

ata tac aag acc ggg caa ccg gct gcg gat cac tac tac agc aag gtc 3346
 Ile Tyr Lys Thr Gly Gln Pro Ala Ala Asp His Tyr Tyr Ser Lys Val
 865 870 875 880

acg gcc acg cgc ctg ctc gcg gcc acc aac agc agg ctg tgc gcg gta 3394
 Thr Ala Thr Arg Leu Leu Ala Ser Thr Asn Ser Arg Leu Cys Ala Al
 885 890 895

 ttc gtc agg gac ggg caa tcg gtc atc gga gcc tgc gcc agc ccg tat 3442
 Phe Val Arg Asp Gly Gln Ser Val Ile Gly Ala Cys Ala Ser Pro Tyr
 900 905 910

 gaa ggc agg tac aga gac atg tac gac gcg ctg cgg cgc ctg ctg tac 3490
 Glu Gly Arg Tyr Arg Asp Met Tyr Asp Ala Leu Arg Arg Leu Leu Tyr
 915 920 925

 atg atc tat atg tcc ggc ctt gcc gta cgc gtc cac gtc agc aag gaa 3538
 Met Ile Tyr Met Ser Gly Leu Ala Val Arg Val His Val Ser Lys Glu
 930 935 940

 gag cag tat tac gac tac gag gac gcc aca ttc cag acc tat gcc ctc 3586
 Glu Gln Tyr Tyr Asp Tyr Glu Asp Ala Thr Phe Gln Thr Tyr Ala Leu
 945 950 955 960

 acc ggc att tcc ctc tgc aac ccg gca gcg tcg ata tgc tgagccgccg 3635
 Thr Gly Ile Ser Leu Cys Asn Pro Ala Ala Ser Ile Cys
 965 970

 gctcggatct gttcgcctgt ccatgttttt ccttgacgga taccgcgaat gaatcccttg 3695
 aaagacttga gagcatcgct accgcgcctg gccttcattg cagcctgcac cctgttgtcc 3755
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<211> 269

<212> PRT

<213> Bordetella pertussis

<400> 6

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Thr Trp Leu Ala Ile Leu Ala Val Thr Ala Pro Val Thr Ser Pro Ala
20 25 30
Trp Ala Asp Asp Pro Pro Ala Thr Val Tyr Arg Tyr Asp Ser Arg Pro
35 40 45
Pro Glu Asp Val Phe Gln Asn Gly Phe Thr Ala Trp Gly Asn Asn Asp
50 55 60
Asn Val Leu Asp His Leu Thr Gly Arg Ser Cys Gln Val Gly Ser Ser
65 70 75 80
Asn Ser Ala Phe Val Ser Thr Ser Ser Ser Arg Arg Tyr Thr Glu Val
85 90 95
Tyr Leu Glu His Arg Met Gln Glu Ala Val Glu Ala Glu Arg Ala Gly
100 105 110
Arg Gly Thr Gly His Phe Ile Gly Tyr Ile Tyr Glu Val Arg Ala Asp
115 120 125
Asn Asn Phe Tyr Gly Ala Ala Ser Ser Tyr Phe Glu Tyr Val Asp Thr
130 135 140
Tyr Gly Asp Asn Ala Gly Arg Ile Leu Ala Gly Ala Leu Ala Thr Tyr
145 150 155 160
Gln Ser Glu Tyr Leu Ala His Arg Arg Ile Pro Pro Glu Asn Ile Arg
165 170 175
Arg Val Thr Arg Val Tyr His Asn Gly Ile Thr Gly Glu Thr Thr Thr
180 185 190
Thr Glu Tyr Ser Asn Ala Arg Tyr Val Ser Gln His Thr Arg Ala Asn
195 200 205
Pro Asn Pro Tyr Thr Ser Arg Arg Ser Val Ala Ser Ile Val Gly Thr
210 215 220
Leu Val Arg Met Ala Pro Val Ile Gly Ala Cys Met Ala Arg Gln Ala
225 230 235 240
Glu Ser Ser Glu Ala Met Ala Ala Trp Ser Glu Arg Ala Gly Glu Ala
245 250 255
Met Val Leu Val Tyr Tyr Glu Ser Ile Ala Tyr Ser Phe
260 265

<210> 7

<211> 226

<212> PRT

<213> Bordetella pertussis

<400> 7

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Leu Ala Leu Leu Gly Ser His Val Ala Arg Ala Ser Thr Pro Gly Ile

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35	40	45
Arg Cys Ala Asn Lys Thr Arg Ala Leu Thr Val Ala Glu Leu Arg Gly		
50	55	60
Ser Gly Asp Leu Gln Glu Tyr Leu Arg His Val Thr Arg Gly Trp Ser		
65	70	75
Ile Phe Ala Leu Tyr Asp Gly Thr Tyr Leu Gly Gly Glu Tyr Gly Gly		
85	90	95
Val Ile Lys Asp Gly Thr Pro Gly Gly Ala Phe Asp Leu Lys Thr Thr		
100	105	110
Phe Cys Ile Met Thr Thr Arg Asn Thr Gly Gln Pro Ala Thr Asp His		
115	120	125
Tyr Tyr Ser Asn Val Thr Ala Thr Arg Leu Leu Ser Ser Thr Asn Ser		
130	135	140
Arg Leu Cys Ala Val Phe Val Arg Ser Gly Gln Pro Val Ile Gly Ala		
145	150	155
Cys Thr Ser Pro Tyr Asp Gly Lys Tyr Trp Ser Met Tyr Ser Arg Leu		
165	170	175
Arg Lys Met Leu Tyr Leu Ile Tyr Val Ala Gly Ile Ser Val Arg Val		
180	185	190
His Val Ser Lys Glu Glu Gln Tyr Tyr Asp Tyr Glu Asp Ala Thr Phe		
195	200	205
Glu Thr Tyr Ala Leu Thr Gly Ile Ser Ile Cys Asn Pro Gly Ser Ser		
210	215	220
Leu Cys		
225		

<210> 8

<211> 131

<212> PRT

<213> Bordetella pertussis

<400> 8

Met Arg Ala Leu Ala Trp Leu Leu Ala Ser Gly Ala Met Thr His Leu		
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Ser Pro Ala Leu Ala Asp Val Pro Tyr Val Leu Val Lys Thr Asn Met		
20	25	30
Val Val Thr Ser Val Ala Met Lys Pro Tyr Glu Val Thr Pro Thr Arg		
35	40	45
Met Leu Val Cys Gly Ile Ala Ala Lys Leu Gly Ala Ala Ala Ser Ser		
50	55	60
Pro Asp Ala His Val Pro Phe Cys Phe Gly Lys Asp Leu Lys Arg Pro		
65	70	75
Gly Ser Ser Pro Met Glu Val Met Leu Arg Ala Val Phe Met Gln Gln		
85	90	95
Arg Pro Leu Arg Met Phe Leu Gly Pro Lys Gln Leu Thr Phe Glu Gly		

100 105 110
 Lys Pro Ala Leu Glu Leu Ile Arg Met Val Glu Cys Ser Gly Ly n
 115 120 125
 Asp Cys Pro
 130

<210> 9
 <211> 120
 <212> PRT
 <213> Bordetella pertussis

<400> 9
 Met His Thr Ile Ala Ser Ile Leu Leu Ser Val Leu Gly Ile Tyr Ser
 1 5 10 15
 Pro Ala Asp Val Ala Gly Leu Pro Thr His Leu Tyr Lys Asn Phe Thr
 20 25 30
 Val Gln Glu Leu Ala Leu Lys Leu Lys Gly Lys Asn Gln Glu Phe Cys
 35 40 45
 Leu Thr Ala Phe Met Ser Gly Arg Ser Leu Val Arg Ala Cys Leu Ser
 50 55 60
 Asp Ala Gly His Glu His Asp Thr Trp Phe Asp Thr Met Leu Gly Phe
 65 70 75 80
 Ala Ile Ser Ala Tyr Ala Leu Lys Ser Arg Ile Ala Leu Thr Val Glu
 85 90 95
 Asp Ser Pro Tyr Pro Gly Thr Pro Gly Asp Leu Leu Glu Leu Gln Ile
 100 105 110
 Cys Pro Leu Asn Gly Tyr Cys Glu
 115 120

<210> 10
 <211> 227
 <212> PRT
 <213> Bordetella pertussis

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 Met Leu Ile Asn Asn Lys Lys Leu Leu His His Ile Leu Pro Ile Leu
 1 5 10 15
 Val Leu Ala Leu Leu Gly Met Arg Thr Ala Gln Ala Val Ala Pro Gly
 20 25 30
 Ile Val Ile Pro Pro Lys Ala Leu Phe Thr Gln Gln Gly Gly Ala Tyr
 35 40 45
 Gly Arg Cys Pro Asn Gly Thr Arg Ala Leu Thr Val Ala Glu Leu Arg
 50 55 60
 Gly Asn Ala Glu Leu Gln Thr Tyr Leu Arg Gln Ile Thr Pro Gly Trp
 65 70 75 80
 Ser Ile Tyr Gly Leu Tyr Asp Gly Thr Tyr Leu Gly Gln Ala Tyr Gly

	85		90		95
Gly Ile Ile Lys Asp Ala Pro	Pro Gly Ala Gly Phe Ile Tyr Arg	Leu			
100		105		110	
Thr Phe Cys Ile Thr Thr Ile Tyr Lys Thr Gly Gln Pro Ala Ala Asp					
115		120		125	
His Tyr Tyr Ser Lys Val Thr Ala Thr Arg Leu Leu Ala Ser Thr Asn					
130		135		140	
Ser Arg Leu Cys Ala Val Phe Val Arg Asp Gly Gln Ser Val Ile Gly					
145		150		155	160
Ala Cys Ala Ser Pro Tyr Glu Gly Arg Tyr Arg Asp Met Tyr Asp Ala					
	165		170		175
Leu Arg Arg Leu Leu Tyr Met Ile Tyr Met Ser Gly Leu Ala Val Arg					
	180		185		190
Val His Val Ser Lys Glu Glu Gln Tyr Tyr Asp Tyr Glu Asp Ala Thr					
	195		200		205
Phe Gln Thr Tyr Ala Leu Thr Gly Ile Ser Leu Cys Asn Pro Ala Ala					
	210		215		220
Ser Ile Cys					
225					

<210> 11
 <211> 976
 <212> PRT
 <213> Bordetella pertussis

<400> 11

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Thr Trp Leu Ala Ile Leu Ala Val Thr Ala Pro Val Thr Ser Pro Ala			
	20	25	30
Trp Ala Asp Asp Pro Pro Ala Thr Val Tyr Arg Tyr Asp Ser Arg Pro			
	35	40	45
Pro Glu Asp Val Phe Gln Asn Gly Phe Thr Ala Trp Gly Asn Asn Asp			
	50	55	60
Asn Val Leu Asp His Leu Thr Gly Arg Ser Cys Gln Val Gly Ser Ser			
	65	70	75
Asn Ser Ala Phe Val Ser Thr Ser Ser Ser Arg Arg Tyr Thr Glu Val			
	85	90	95
Tyr Leu Glu His Arg Met Gln Glu Ala Val Glu Ala Glu Arg Ala Gly			
	100	105	110

Arg Gly Thr Gly His Phe Ile Gly Tyr Ile Tyr Glu Val Arg Ala Asp
 115 120 125

Asn Asn Phe Tyr Gly Ala Ala Ser Ser Tyr Phe Glu Tyr Val Asp Thr
 130 135 140

Tyr Gly Asp Asn Ala Gly Arg Ile Leu Ala Gly Ala Leu Ala Thr Tyr
 145 150 155 160

Gln Ser Glu Tyr Leu Ala His Arg Arg Ile Pro Pro Glu Asn Ile Arg
 165 170 175

Arg Val Thr Arg Val Tyr His His Gly Ile Thr Gly Glu Thr Thr Thr
 180 185 190

Thr Glu Tyr Ser Asn Ala Arg Tyr Val Ser Gln Gln Thr Arg Ala Asn
 195 200 205

Pro Asn Pro Tyr Thr Ser Arg Arg Ser Val Ala Ser Ile Val Gly Thr
 210 215 220

Leu Val Arg Met Ala Pro Val Ile Ser Ala Cys Met Ala Arg Gln Ala
 225 230 235 240

Glu Ser Ser Glu Ala Met Ala Ala Trp Ser Glu Arg Ala Gly Glu Ala
 245 250 255

Met Val Leu Val Tyr Tyr Glu Ser Ile Ala Tyr Ser Phe Val Met Pro
 260 265 270

Ile Asp Arg Lys Thr Leu Cys His Leu Leu Ser Val Leu Pro Leu Ala
 275 280 285

Leu Leu Gly Ser His Val Ala Arg Ala Ser Thr Pro Gly Ile Val Ile
 290 295 300

Pro Pro Gln Glu Gln Ile Thr Gln His Gly Ser Pro Tyr Gly Arg Cys
 305 310 315 320

Ala Asn Lys Thr Arg Ala Leu Thr Val Ala Glu Leu Arg Gly Ser Gly
 325 330 335

Asp Leu Gln Glu Tyr Leu Arg His Val Thr Arg Gly Trp Ser Ile Phe
 340 345 350

Ala Leu Tyr Asp Gly Thr Tyr Leu Gly Gly Glu Tyr Gly Gly Val Ile
 355 360 365

Lys Asp Gly Thr Pro Gly Gly Ala Phe Asp Leu Lys Thr Thr Phe Lys
 370 375 380

Ile Met Thr Thr Ala His Thr Gly Gln Pro Ala Thr Asp His Val Tyr
 385 390 395 400

Ser His Val Thr Ala Thr Arg Leu Leu Ser Ser Thr His Ser Arg Leu
 405 410 415

Cys Ala Val Phe Val Arg Ser Gly Gln Pro Val Ile Gly Ala Cys Thr
 420 425 430

Ser Pro Tyr Asp Gly Lys Tyr Trp Ser His Tyr Ser Arg Leu Arg Lys
 435 440 445

Met Leu Tyr Leu Ile Tyr Val Ala Gly Ile Ser Val Arg Val His Val
 450 455 460

Ser Lys Glu Glu Gln Tyr Tyr Asp Tyr Glu Asp Ala Thr Phe Glu Thr
 465 470 475 480

Tyr Ala Leu Thr Gly Ile Ser Ile Cys His Pro Gly Ser Ser Leu Cys
 485 490 495

Val Ala Trp Leu Leu Ala Ser Gly Ala Met Thr His Leu Ser Pro Ala
 500 505 510

Leu Ala Asp Val Pro Tyr Val Leu Val Lys Thr His His Val Val Thr
 515 520 525

Ser Val Ala His Lys Pro Val Glu Val Thr Pro Thr Arg Met Leu Val
 530 535 540

Cys Gly Ile Ala Ala Lys Leu Gly Ala Ala Ala Ser Ser Pro Asp Ala
 545 550 555 560

His Val Pro Phe Cys Phe Gly Lys Asp Leu Lys Arg Pro Gly Ser Ser
 565 570 575

Pro His Glu Val Met Leu Arg Ala Val Phe Met Gln Gln Arg Pro Leu
 580 585 590

Arg Met Phe Leu Gly Pro Lys Gln Leu Thr Phe Glu Gly Lys Pro Ala
 595 600 605

Leu Glu Leu Ile Arg Met Val Glu Cys Ser Gly Lys Gln Asp Cys Pro
 610 615 620

Val Phe Met His Thr Ile Ala Ser Ile Leu Leu Ser Val Leu Gly Ile
 625 630 635 640
 Tyr Ser Pro Ala Asp Val Ala Gly Leu Pro Thr His Leu Tyr Lys Asn
 645 650 655
 Phe Thr Val Gln Glu Leu Ala Leu Lys Leu Lys Gly Lys Asn Gln Glu
 660 665 670
 Phe Cys Leu Thr Ala Phe His Ser Gly Arg Ser Leu Val Arg Ala Cys
 675 680 685
 Leu Ser Asp Ala Gly His Glu His Asp Thr Trp Phe Asp Thr Met Leu
 690 695 700
 Gly Phe Ala Ile Ser Ala Tyr Ala Leu Lys Ser Arg Ile Ala Leu Thr
 705 710 715 720
 Val Glu Asp Ser Pro Tyr Pro Gly Thr Pro Gly Asp Leu Leu Glu Leu
 725 730 735
 Gln Ile Cys Pro Leu Asn Gly Tyr Cys Glu Val Phe Met Leu Ile Asn
 740 745 750
 Asn Lys Lys Leu Leu His His Ile Leu Pro Ile Leu Val Leu Ala Leu
 755 760 765
 Leu Gly Met Arg Thr Ala Gln Ala Val Ala Pro Gly Ile Val Ile Pro
 770 775 780
 Pro Lys Ala Leu Phe Thr Gln Gln Gly Gly Ala Tyr Gly Arg Cys Pro
 785 790 795 800
 Asn Gly Thr Arg Ala Leu Thr Val Ala Glu Leu Arg Gly Asn Ala Glu
 805 810 815
 Leu Gln Thr Tyr Leu Arg Gln Ile Thr Pro Gly Trp Ser Ile Tyr Gly
 820 825 830
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 Asp Ala Pro Pro Gly Ala Gly Phe Ile Tyr Arg Glu Thr Phe Cys Ile
 850 855 860
 Thr Thr Ile Tyr Lys Thr Gly Gln Pro Ala Ala Asp His Tyr Tyr Ser
 865 870 875 880

Lys Val Thr Ala Thr Arg Leu Leu Ala Ser Thr Asn Ser Arg Leu Cys
 885 890 895
 Ala Val Phe Val Arg Asp Gly Gln Ser Val Ile Gly Ala Cys Ala Ser
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 Pro Tyr Glu Gly Arg Tyr Arg Asp His Tyr Asp Ala Leu Arg Arg Leu
 915 920 925
 Leu Tyr Met Ile Tyr Met Ser Gly Leu Ala Val Arg Val His Val Ser
 930 935 940
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